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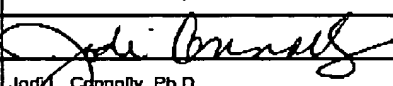
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| TRANSMITTAL FORM <small>(to be used for all correspondence after initial filing)</small> | Application Number | 10/719,370 |
| | Filing Date | 11/21/2003 |
| | First Named Inventor | Donna T. Ward |
| | Art Unit | 1635 |
| | Examiner Name | Jane J. Zara |
| | Attorney Docket Number | ISPT1010 (PTS-0070US.P1) |
| Total Number of Pages in This Submission | | 11 |

| ENCLOSURES (Check all that apply) | | |
|--|--|---|
| <input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): Preliminary Amendment |
| Remarks _____ | | |

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | | | |
|--------------|---|----------|--------|
| Firm Name | Isis Pharmaceuticals, Inc. | | |
| Signature |  | | |
| Printed name | Jodi L. Connolly, Ph.D. | | |
| Date | 10/27/05 | Reg. No. | 54,044 |

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CENTRAL FAX CENTER****OCT 27 2005****DOCKET NO.: ISPT1010 (PTS-0070US.P1)****PATENT****IN THE UNITED STATES PATENT AND TRADEMARK OFFICE****Applicants: Ward et al.****Confirmation No.: 3593****Serial No.: 10/719,370****Group Art Unit: 1635****Filed: November 21, 2003****Examiner: Zara, Jane J.****Title: MODULATION OF HIF1(ALPHA) AND HIF2(ALPHA) EXPRESSION**

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On October 27, 2005


Laura Eames

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

PRELIMINARY AMENDMENT

Preliminary to examination of the above-captioned patent application, please amend the application as follows:

- ☐ Amendments to the Specification begin on page this paper.
- ☒ Amendments to the Claims are reflected in the listing of the claims which begins on page 2 of this paper.
- ☐ Amendments to the Drawings begin on page of this paper and include an attached replacement sheet.
- ☒ Remarks/Arguments begin on page 10 of this paper.